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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/991,445	11/16/2001	Ernest G. Schutt	ALLIA.62F1C1C1	3983
48394	7590	09/29/2006	EXAMINER	
DIEHL SERVILLA LLC 77 BRANT AVE SUITE 110 CLARK, NJ 07066			CHONG, YONG SOO	
			ART UNIT	PAPER NUMBER
			1617	

DATE MAILED: 09/29/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/991,445	SCHUTT ET AL.	
	Examiner	Art Unit	
	Yong S. Chong	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 10 July 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-10, 12-14 and 16-20 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-10, 12-14, 16-20 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of the Application

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 7/10/2006 has been entered.

Claim(s) 11 and 15 have been cancelled. Claim(s) 1-10, 12-14, 16-20 are pending. Claim(s) 1, 10, 17 have been amended. Claim(s) 1-10, 12-14, 16-20 are examined herein.

Applicant's arguments have been fully considered but found not persuasive. The rejections of the last Office Action are maintained for reasons of record and are repeated below for Applicant's convenience.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

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Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-10, 12-20 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims of 1-12 of US Patent 6,372,195, claims 1-101 of US Patent 6,258,339, claims 1-24 of US Patent 5,695,741, claims 1-38 of US Patent 5,639,443, and claims 17-22 of US Patent 5,798,091, claims 1-9, 38-73 of US Patent 5,804,162, claims 26-51 of US Patent 6,193,952 for the reasons or record.

Response to Arguments

Applicant's request to revisit this rejection after the claims have been formally allowed is noted.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham vs John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.

3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-10, 13-18, 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schneider et al US Patent 5,413,774.

The instant claims are directed microbubbles comprising at least one fluorocarbon gas and at least one modifier gas that can comprise oxygen. The scope of the instant limitation "modifier gas" is described in paragraphs 0034, 0061-0069.

Accordingly, the scope of the term "a modifier gas" is inclusive and encompasses other gases such as oxygen, air, perfluorocyclooctane, perfluoropentane, perfluoroethane and perfluoromethane. The instant claims further require a ratio of the modifier gas to the fluorocarbon gas in the ranges of 1:100 to about 1000:1.

Schneider meets the limitations of the claimed microbubbles. Schneider teaches gas filled microvesicles that can contain a mixture of a first perfluorocarbon gas such as perflorobutane (C₄F₁₀) and a secondary gas such as air which contains oxygen, nitrogen, CO₂. (see col 5, lines 50-56., examples 7-8", claims 1-2, col 14, lines 45, 68). The second gas of Schneider can include other perfluorocarbons such as perfluoromethane or perfluorethane. (see (col 14, lines 42-49). Schneider also teaches a membrane around his microvesicles (see claims 5-9).

Schneider's fluorocarbon is the same as those instantly claimed; therefore, it possesses the same functional characteristics as the instant fluorocarbon. Air, nitrogen and the like gases including other perfluorocarbons also fall within the instant genus of modifier gases. Thus, the microbubbles of Schneider contains a perfulorobutane. The

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microbubbles of Schneider also comprise a secondary gas including air, perfluormethane, which meets the instant limitation "modifier gas."

Schneider's microbubbles comprise a membrane comprising phospholipids or albumin (see col 13-14). Schneider administers his microvesicles to Rabbits thus exposing them to an external medium comprising blood and other physiological gases such as air or oxygen. (see examples 2-4, cols 9-11). Thus, Schneider meets all structural limitations of the instant claims and all functional limitations of the instant claims.

Schneider only fails to specifically recite the instantly claimed ranges of modifier gas to fluorocarbon gas.

However, absent a showing of unexpected results, it would have been obvious to one of ordinary skill in the art at the time of invention to optimize the concentrations of individual gases in Schneider's microbubbles by routine experimentation to observe the most effective clinical results.

Claims 12, 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schneider et al US Patent 5,413,774 in view of Tickner US Patent 4,265,251.

The teachings of Schneider are described above. Schneider only fails to incorporate delivery of oxygen in his microbubbles.

Tickner teaches methods of ultrasound imaging using gas containing microbubbles wherein the gas is oxygen (abstract, col 7, lines 11-54). Tickner teaches that although the preferred gas is carbon dioxide, however, other gases such as freons and oxygen may be used in his contrast agents (col 6, lines 63-67)..

Although Schneider fails to use oxygen with pefluorobutane in his gaseous mixtures compositions, he specifically teaches that any gas like air and nitrogen can be employed in his gaseous mixture. Tickner shows that for the purposes of ultrasonic contrast agents, gases such as oxygen, nitrogen, and Freons are substantially interchangeable and are functional equivalents.

Thus, absence of showing unexpected results, it would have been obvious to one of ordinary skill in the art at the time of invention to substitute one of air or nitrogen gases in Schneider's microvesicles with oxygen and create a microvesicle that contains pefluorobutane and oxygen, because as shown by Tickner, oxygen is considered art recognized equivalents to suitable gases enumerated by Schneider. Subsequently, the ordinary skill in the art would have had a reasonable expectation of success in mixing perfluorobutane with oxygen to produce a gaseous microvesicles.

Claims 1-10, 12-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schneider in view of Clark US Patent 5,536,753.

The teachings of Schneider are described above. Schneider does not specifically uses oxygen in his gaseous mixture.

Clark is used to show that perflouorocarbon containing emulsions are safe oxygen transport agents. (see abstract). Clark also teaches the use of emulsifying agents such as phospholipids and polymeric agents that can entrap the gas within his formulation (see col 2, lines 43-55). Clark further employs such fluorocarbons as perfluoromethylcyclohexanes that fall within the scope of the instantly claimed perfluorocyclohexanes (see col 2, lines 39 and col 4, lines 60-64). Clark further

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elaborates on suitable concentrations of perfluorocarbon, the surfactant and the oxygen (see col 3-4; specifically col 3, lines 23-65).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time of invention to utilize a mixture of a perfluorocarbon with oxygen, because as suggested by Schneider and Clark, the ordinary skill in the art would have had a reasonable expectation of success in preparing microbubble for in vivo delivery of oxygen. Absence of showing unexpected results, one of ordinary skill in the art would have had a reasonable expectation of success for optimizing the concentrations of perfluorocarbon and oxygen for effective clinical or diagnostic use, when mixing the perfluorocarbon with oxygen.

Response to Arguments

Applicant argues that some of the fluorocarbons, such as CHClF_2 and Freon F-21, do not fit the criteria set forth by Schneider et al. This is not persuasive because perfluorobutane was selected as the elected species of fluorocarbons and oxygen as the modifier gas. Currently, the claims are not directed to CHClF_2 and Freon F-21. Nonetheless, the standard for a case of obviousness is not absolute but a reasonable expectation of success.

Applicant argues that Schneider et al. does not disclose optimizing the ratio of gases, therefore teaches away from the present invention. This is not persuasive because claim 2 discloses an atmosphere of a first gas and then substantially substituting at least a fraction of said first gas with a second gas. Accordingly, it is obvious to optimize the ratio of gases when the general conditions are disclosed.

Generally, mere optimization of ranges will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "When the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimal or workable ranges by routine experimentation. *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955); see also *In re Peterson*, 315 F. 3d at 1330, 65 USPQ 2d at 1382 "The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages." MPEP 2114.04.

Applicant argues that the criteria of Schneider et al. does not recognize that mole fractions of gases within a microbubble accounts for the partial pressure and diffusion of gases in microbubble stabilization. Applicant also argues that Schneider et al. does not mention that an osmotically stabilized microbubble grows and shrinks in response to the gas saturation levels of the surrounding medium. This is not persuasive because a composition and its properties are inseparable.

"Products of identical chemical composition can not have mutual exclusive properties." Any properties exhibited by or benefits from are not given any patentable weight over the prior art provided the composition is inherent. A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the disclosed properties are necessarily present. *In re Spada*, 911 F.2d 705, 709, 15 USPQ 1655, 1658 (Fed. Cir. 1990). See MPEP 2112.01. The

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burden is shifted to the applicant to show that the prior art product does not inherently possess the same properties as the instantly claimed product.

Applicant argues that gases such as oxygen, nitrogen, and Freon are not substantially interchangeable and functionally equivalent. This is not persuasive because Schneider et al. clearly discloses air, which is composed of nitrogen and oxygen. Moreover, Tickner et al. discloses that oxygen may be used as a contrast agent.

Applicant argues that the liquid emulsions disclosed by Clark et al. are very different from the gas microbubbles of the present invention. This is not persuasive because the Clark et al. reference was only incorporated in the rejection because of the disclosure that perfluorocarbons containing emulsions are safe oxygen transport agents.

In response to applicant's arguments against the references, one cannot show nonobviousness by attacking references individually where the rejections are based on the combination of references. See *In re Keller*, 642 F. 2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F. 2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Conclusion

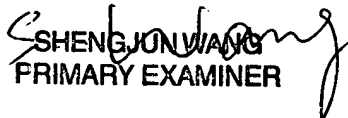
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong S. Chong whose telephone number is (571)-272-8513. The examiner can normally be reached on M-F, 9-6.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, SREENI PADMANABHAN can be reached on (571)-272-0629. The fax phone number for the organization where this application or proceeding is assigned is (571)-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

YSC


SHENGJUN WANG
PRIMARY EXAMINER